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Predictors of Complications after Breast Reconstruction Surgery: A Systematic Review and Meta-analysis

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Background: Breast reconstruction (BR) is a unique surgical procedure that provides patients undergoing mastectomy with significant psychosocial and aesthetic benefits and has also become a crucial part of the treatment pathway for women with breast cancer. Due to methodological inadequacies and the absence of substantial risk factor analysis, no conclusion can be drawn about the correlation between risk variables and post-surgical complications in BR surgery. We aim to identify the potential risk factors associated with postoperative complications.

Methods: We queried MEDLINE and Cochrane CENTRAL from their inception to March 2022, for published randomized controlled trials and observational studies that assessed complications post-reconstruction procedure in breast cancer patients following mastectomy or evaluated at least one of the following outcomes of major or reoperative complications. The results from the studies were presented as odds ratios with 95% confidence intervals and were pooled using a random-effects model.

Results: Our pooled analysis demonstrated a significant correlation with BR postoperative complications and risk factors such as diabetes, hypertension, and obesity. Diabetes and the development of seroma were found to have a significant relationship. Risk variables such as age, radiotherapy, COPD, and smoking had no significant connection with 0-to-30-day readmission and 30-to-90-day readmission.

Conclusion: This meta-analysis shows that risk factors like age, smoking history, high blood pressure, and body mass index (BMI) have a big effect on complications after BR, and patients with risk factors have a high rate of developing infection.
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INTRODUCTION

Breast reconstruction (BR) is a unique surgical procedure that provides patients undergoing mastectomy with significant psychosocial and aesthetic benefits and has also become a crucial part of the treatment pathway for women with breast cancer.[1–3] Over the past two decades, the number of BR surgeries has climbed steadily. In 2016, the American Society of Plastic Surgeons reported that more than 109,256 BR procedures were performed in the United States alone.[4]

BR includes two primary techniques: autologous reconstruction and tissue expander/implant reconstruction.[5] The American Society of Plastic Surgeons has separate guidelines for both of these techniques.[6,7] Neither of these treatments favors one approach over the other, despite the fact that tissue expander/implant reconstruction is utilized more frequently and autologous reconstruction can create a natural and symmetric breast mound that provides greater psychosocial benefits than implant reconstruction.[8] Because BR is an elective surgery, the risks and

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advantages must be thoroughly weighed before surgery. According to both guidelines, there is no standard surgery for BR, and the ultimate judgment regarding the care of a particular patient must be made by the physician, considering patient preferences, risk factors, and available resources.[6,7]

Both BR procedures include risks, including the possibility of complications. In autologous BR, skin necrosis and wound dehiscence are frequent abdominal site complications, but in tissue expander/implant BR, infection, seroma, and hematoma are common.[9–12] In the past, studies have evaluated risk factors for these complications, such as age, obesity, high blood pressure, diabetes, and smoking.[11–13] However, the generalizability and validity of prior studies have been impeded by a variety of methodological concerns, such as a small sample size, the absence of a control group, insufficient patient follow-up, and a lack of extensive risk factor analysis, making it difficult to draw conclusions regarding the association between risk factors and postsurgical complications in BR.

As part of the informed consent process, there is an increasing demand for precise and individualized preoperative risk assessment. In modern cancer care, the provision of correct information regarding the risks and benefits of treatment has been designated as a top priority. Comprehensive awareness of the risk factors that lead to complications to counsel patients correctly and guide the joint decision-making process with reliable information is necessary. Scarcity of techniques available to assist plastic surgeons in assessing preoperative risk before BR contributes to ambiguity in the effectiveness of the procedure.[14] The most widely used instrument, the American College of Surgeons National Surgical Quality Improvement Program Surgical Risk Calculator, lacks the discriminatory power to identify patients with a higher risk of problems during BR,[15,16] necessitating further research into the associations between risk factors and postoperative complications, which can also aid in developing an effective tool for risk assessment. In this study, we aimed to pool all studies reporting data on risk factors and postoperative complications and conduct a meta-analysis to examine the evidence pertaining to any potential correlations between risk factors and postoperative complications.

Takeaways

Question: What are the predictors of complications following breast reconstruction (BR) surgery?

Findings: This meta-analysis shows that risk factors like age, smoking history, high blood pressure, and body mass index (BMI) have a big effect on complications after BR, and patients with risk factors have a high rate of developing infection.

Meaning: Surgeons must be knowledgeable of such predictors before performing BR on their patients, to avoid unwanted complications.

METHODS

This meta-analysis was performed in accordance with the Preferred Reporting Items for Systematic review and Meta-Analyses guidelines.[17] No ethical review board permission was required for this analysis because the data were widely available.

Data Sources and Strategy

We systematically searched two databases (MEDLINE and Cochrane CENTRAL) from inception to March 2022, without any time or language restrictions, using a detailed search strategy involving all possible synonymous terms of breast augmentation and abbreviations, along with MeSH terms and Boolean operators "AND" and "OR." The search strategy is included in Supplemental Digital Content 1. (**See appendix, Supplemental Digital Content 1,** which displays the supplementary material. **http://links.lww.com/PRSGO/C296**.)

Study Selection

The studies retrieved from our literature search were cross-verified by two independent investigators and exported to Endnote Reference Library (Version X7.5; Clarivate Analytics, Philadelphia, PA) software where duplicates were sought and removed. The full texts of the remaining studies were thoroughly read to confirm their relevance. Any disagreements regarding study selection were resolved by mutual consensus with a senior investigator (TSJ). The predefined eligibility criteria for our meta-analysis were (a) randomized controlled trials or observational studies; (b) assessed complications post reconstruction procedure in breast cancer patients following mastectomy; (d) evaluated at least one of the following outcomes of major or reoperative complications, hospitalization, seroma, or infection.

Data Extraction

For outcomes of interest, odds ratios (ORs) were extracted. In those studies where only raw data were reported, summary events were proportionated to calculate ORs with 95% confidence intervals (CIs). Furthermore, study characteristics and patient baseline characteristics were also extracted and are reported in **Supplemental Digital Content 1** (**http://links.lww.com/PRSGO/C296**).

Statistical Analysis

All statistical analyses were carried out using RevMan (version 5.3; Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration). The forest plots of relevant outcomes were visually developed after the ORs with 95% CIs were pooled using the random-effects model.[18] These outcomes were then stratified into several subgroups based on the type of predictor and subsequently, the $\chi 2$ test was performed to evaluate the differences between the subgroups. The I^2 test was performed to examine the heterogeneity in the study outcomes. An I^2 score of 50% was assumed to indicate a high amount of heterogeneity.[19] A P value less than or equal to 0.05 was considered significant for all the above analyses.

RESULTS

Search Results and Study Characteristics

The initial literature search yielded 7363 results. After screening for titles and abstracts, and reviewing full-text articles, 33 studies were short-listed.[4,9,10,12–15,20–45] The Preferred Reporting Items for Systematic review and Meta-Analyses flowchart summarizes the results of our literature search. (**See figure, Supplemental Digital Content 2**, which displays the Preferred Reporting Items for Systematic review and Meta-Analyses flowchart. **http://links.lww.com/PRSGO/C297**.)

The finalized studies included over 100,000 patients. The overall patient population included patients undergoing BR following mastectomy. BR techniques primarily involved implants, tissue-expander, and autologous reconstructions, including transverse rectus abdominis myocutaneous flaps, latissimus dorsi flaps, and deep inferior epigastric perforator flaps. In these patients, predictors of complications were assessed.

RESULTS OF META-ANALYSIS

The summarized results of meta-analysis are presented in Supplemental Digital Content 3. (**See table, Supplemental Digital Content 3**, which displays the summary of meta-analysis. **http://links.lww.com/PRSGO/C298**.)

OUTCOMES

Multiple Complications

Of the 33 selected studies, 18 reported data on multiple complications. Predictors of any complication following BR (including risk factors like diabetes, chronic obstructive pulmonary disease [COPD], hypertension), and patient characteristics such as age, obesity, and smoking were assessed. These predictors were significantly associated with a higher probability of developing complications after BR (OR: 1.52; CI [1.39, 1.66], I^2 84%, $P < 0.00001$) (**SDC1: Figure S1** [**http://links.lww.com/PRSGO/C296**]). Subgroup analysis revealed significant subgroup differences between the risk factors ($P < 0.00001$).

Major or Reoperative Complication

Of the 33 selected studies, 14 reported data on predictors of major or reoperative complications following BR, including risk factors like diabetes, COPD, hypertension, age, obesity, and smoking. These predictors were significantly associated with a higher probability of developing complications after BR (OR: 1.05; CI [1.02, 1.18], I^2 59%, $P = 0.0001$, **SDC1: Figure S2** [**http://links.lww.com/PRSGO/C296**]). According to subgroup analysis, positive subgroup differences were observed between the risk factors ($P < 0.00001$).

Readmission

0-to-90-Day Readmission

Of the 33 selected studies, two studies reported data for 0-to-90-day readmission. Our pooled analysis yielded significant relation (OR: 1.57; CI [0.78, 2.82], I^2 76%, $P = 0.001$, **SDC1: Figure S3** [**http://links.lww.com/PRSGO/C296**]). Multiple predictors such as obesity (OR: 2.19; CI [1.65, 2.91], $P < 0.00001$), diabetes (OR: 1.59; CI [1.30, 1.95], $P < 0.00001$), hypertension (OR: 1.65; CI [1.06, 2.57], $P < 0.03$) and smoking (OR: 2.13; CI [1.05, 4.34], $P < 0.04$) reported significant results with risk of 0-to-90-day readmission. Subgroup differences were reportedly significant ($P = 0.01$).

0-to-30-Day Readmission

Of the 33 selected studies, two studies reported data for 0-to-30-day readmission. Our pooled analysis yielded significant results for 0-to-30-day readmission (OR: 1.63; CI [1.26, 2.10], I^2 87%, $P = 0.0002$, **SDC1: Figure S4** [**http://links.lww.com/PRSGO/C296**]). Age (OR: 1.01; CI [0.98, 1.04], $P = 0.52$), radiotherapy (OR: 1.51; CI [0.78, 2.92], $P = 0.22$), COPD (OR: 1.62; CI [0.58, 4.49], $P = 0.36$) and smoking (OR: 1.67; CI [0.83, 3.33], $P = 0.15$) reported no significant association with risk of 0-to-30-day readmission. Subgroup differences were reportedly significant ($P = 0.01$).

30-to-90-Day Readmission

Of the 33 selected studies, two studies reported data on for 30-to-90-day readmission. Our pooled analysis revealed significant results for 30-to-90-day readmission (OR: 1.30; CI [1.04, 1.35], I^2 58%, $P = 0.02$, **SDC1: Figure S5** [**http://links.lww.com/PRSGO/C296**]). Individual predictors, including age (OR: 1.10; CI [0.97, 1.33], $P = 1.00$), hypertension (OR: 0.98; CI [0.69, 1.40], $P = 0.91$), COPD (OR: 1.01; CI [0.64, 1.59], $P = 0.91$), smoking (OR: 2.56; CI [0.95, 6.86], $P = 0.06$), and radiotherapy (OR: 2.01; CI [0.81, 4.99], $P = 0.13$), showed nonsignificant results. Subgroup analysis yielded positive subgroup differences ($P = 0.02$).

Seroma

The correlation between individual predictor and the development of seroma was studied. Our analysis showed a significant association between diabetes and development of seroma (OR: 1.51; CI [1.02, 2.24], I^2 0%, $P = 0.04$, **SDC1: Figure S6** [**http://links.lww.com/PRSGO/C296**]).

Infection

Of the 33 selected studies, four reported data on infection rates after BR. A statistically significant association was reported between predictors and risk of infection subsequent to BR (OR: 1.43; CI [1.16, 1.76], I^2 67%, $P<0.001$, **SDC1: Figure S7** [**http://links.lww.com/PRSGO/C296**]). Age (OR: 1.03; CI [0.91, 1.16], $P = 0.67$), radiotherapy (OR: 2.67; CI [0.48, 14.34.], $P = 0.26$), diabetes (OR: 1.44; CI [0.84, 2.48], $P = 0.19$), COPD (OR: 1.05; CI [0.76, 1.45], $P = 0.77$), and smoking (OR: 1.52; CI [0.98, 2.36], $P = 0.06$) did not suggest significant results.

DISCUSSION

In our meta-analysis of more than 100,000 patients, our findings suggest a significant correlation between postoperative complications of BR and risk factors, including comorbid conditions such as diabetes, COPD, hypertension, and patient characteristics such as age, obesity, and smoking. Moreover,

significant relationship was observed between diabetes and the development of seroma. We found that individual predictors such as age, radiotherapy, COPD, and smoking had no significant association with 0-to-30-day readmission. Similarly, these risk factors had no significant correlation with 30-to-90-day readmission. On the contrary, multiple predictors, including obesity, diabetes, and hypertension and smoking, significantly impacted 0-to-90-day readmission. Moreover, our results also show that patients with risk factors were more vulnerable to developing an infection after BR surgery. Our findings are notable because they reinforce the role of the above-mentioned predictors in postoperative complications.

Our findings indicate that age, obesity, and smoking are significant predictors of major or reoperative complications. These results are consistent with those of a previous retrospective study involving 376 patients, which concluded that age and smoking history played a significant role in the development of postoperative complications.[22] Similarly, in another study with 912 individuals, those who were both obese and smokers had a 12-fold increase in problems.[14] In contrast, a prospective multicenter study conducted in the United States indicated that age has no significant effect on the incidence of complications.[46] Similarly, another study found no significant difference in flap failure rates between patients with a normal BMI and obese individuals.[15] The disparities in results were attributed to variations in study methodology, which included differences in BR techniques and baseline characteristics of the included population.

Cigarette smoking has been linked for a long time as a risk factor for problems in tissue expander-based reconstruction. Numerous studies have revealed that smokers are at a higher risk for problems, particularly mastectomy flap necrosis.[47,48] These results owe to nicotine's deleterious effects on blood flow,[48] which can be significant in tissues with reduced blood flow, such as mastectomy flaps. Similarly, obesity has been highlighted as a risk factor for problems associated with tissue expander-based BR.[49] This might be due to the fact that obese women tend to have proportionately larger breast size, necessitating a more thorough dissection and resulting in larger and longer mastectomy flaps. Compared with shorter flaps, longer flaps have a diminished blood flow, which increases the risk of complications in these individuals. In addition, these patients have more postoperative dead space and longer operational periods, which might elevate the risk of problems.[22] Age can be regarded an independent predictor of complications due to the fact that older people have thinner skin than younger ones.[50] In light of the fact that the process of tissue expansion exerts pressure on the mastectomy flaps, smaller flaps may be less resistant to extrusive pressures than broader flaps, and hence, may be more susceptible to extrusions. In addition, older patients often have a greater number of medical comorbidities than younger patients, which might further impact the incidence of complications.[22]

Our findings also report that patients with risk factors such as hypertension and obesity are more susceptible to infection after BR surgery. This result is consistent with previous literature where individuals with obesity and high blood pressure were more likely to get surgical-site infections.[4] Higher chances of hematoma development after surgery may be the cause of hypertension's impact on surgical-site infection. As previously demonstrated, in individuals with hypertension, the functional and structural alterations to the microcirculation may have a greater effect on the perfusion of the mastectomy skin flap.[51] It is notable that people with hypertension frequently also have obesity, which has been found to impair tissue microcirculation. However, hypertension could be a more manageable risk factor in the perioperative period than obesity, which calls for long-term lifestyle changes or weight loss. Blood pressure must be kept under control throughout the preoperative period to avoid peripheral tissue vasoconstriction and to reduce the risk of postoperative hemorrhage.[4] Topical nitroglycerin treatment on mastectomy skin flaps is one method to investigate. Several studies, including a randomized controlled trial, have demonstrated that this technique reduces mastectomy flap necrosis.[52,53]

There are numerous studies that review the postoperative complications associated with BR, such as a previously published meta-analysis that compared the risk of complications in immediate BR and delayed reconstruction but did not focus on the risk factors that lead to those complications.[54] Therefore, there are few studies that investigate the risk factors for these events. Our meta-analysis is, to the best of our knowledge, the first original study to demonstrate the involvement of several parameters in predicting complications after BR surgery. It is crucial that surgeons and patients have a thorough understanding of potential problems. The individual impact of risk factors must be assessed in the context of the oncologic and surgical requirements of each patient. Although most of these risk variables are not open to intervention, they may help surgeons to take the necessary measures in a timely manner while providing patients with more precise information about their susceptibility to postoperative problems.[55] Surgeons and patients can make better informed decisions toward the aim of a successful BR by taking into account the risks mentioned in this study. Moreover, it is essential for excellent practice to reevaluate current procedures and modify or alter them based on novel research. Our findings regarding association between risk variables and postoperative complications can also assist in the revision of existing guidelines.

There are certain limitations to our meta-analysis. First, some risk factors, such as diabetes and readmission, and certain complications, such as seroma, are underrepresented. Other complications, such as capsular contracture, are not included in our research owing to a lack of data, which may mitigate the effects of our findings. Second, we did not examine predictors of complications associated with a particular BR technique; thus, future research is required to investigate the correlation of risk factors with complications associated with a particular BR technique. Thirdly, there was heterogeneity among included studies due to differences in sample populations and study settings, so an analysis was conducted using the random-effects model for this purpose.

CONCLUSIONS

Our study concludes that risk variables such as age, smoking history, hypertension, and BMI had a significant

influence on postoperative complications following BR. In the future, further research is warranted with a larger sample size to evaluate the determinants of complications in specific types of BR operations. In addition, measures for controlling modifiable risk factors can be considered because BR surgery seems to be essential for raising patients' confidence and enhancing their quality-of-life following mastectomy.

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